

Cephalosporins*

Overview

More than twenty cephalosporin antimicrobials are currently used in medicine. This group of β -lactams was introduced for clinical use in the 1960s. The cephalosporins are derived from 7-aminocephalosporanic acid and are weak acids. Modifications of this acid nucleus and semisynthetic sidechain substitutions produce differences in antibacterial spectra, β -lactamase sensitivities and pharmacokinetics in the respective cephalosporins. Cephalosporin antimicrobials are bactericidal, relatively non-toxic and are characterized by very good pharmacokinetic properties. Their chemical properties are similar to the penicillins, but cephalosporins are slightly more stable to pH and temperature changes. In veterinary medicine these antimicrobials are most often used in treatment of bacterial dermatitis, osteomyelitis, prostatitis and arthritis. These drugs are also used commonly to treat urinary infections that are not caused by *P aeruginosa*.

The mode of action of cephalosporins is similar to that of the penicillins. Like the penicillins, cephalosporins bind to penicillin binding proteins and interfere with cell wall enzymes. Major adverse reactions to cephalosporins are also similar to those experienced with penicillin. The incidence of primary allergic reactions is between 1% and 3 %. The rate of cross hypersensitivity with penicillin is about 10%.

First generation cephalosporins (cephalothin, cephaloridine, cephapirin, cefazolin, cephalixin, cephadrine, cefadroxil) are most effective against aerobic Gram-positive cocci, such as methicillin sensitive *Staphylococcus aureus* and are effective against several Gram-negatives, such as *E coli*, *Proteus*, *Klebsiella*, *Salmonella*, *Shigella* and *Enterobacter* species. These first generation antimicrobials are generally susceptible to β -lactamases and are not as effective against anaerobes as the penicillins. Although the cost of cephalosporins often precludes their use in veterinary medicine, first generation cephalosporins are very useful in treatment of infections, such as dermatitis involving *Staphylococcus* species. In pediatrics, oral cephalixin and parenteral cefazolin are the most commonly used first generation cephalosporins. The two drugs are used primarily for skin and soft tissue infections caused by streptococci and *S aureus*, and bacterial endocarditis caused by *Streptococcus viridans* and *S aureus*. Higher doses of cefazolin and cephalixin are used to treat bone and joint infections in children. First generation cephalosporins are also utilized in the treatment of open fractures, lymphadenitis, abscesses, pharyngitis and necrotizing fasciitis. In veterinary medicine cephalixin and cefadroxil are the most commonly used oral preparations.)

Second generation cephalosporins (cepfamandole, cefoxitin, cefotiam, cefaclor, cefuroxime, cefotetan, ceforanide, cefonicid, cefprozil, cefoxitin, cefotetan, cefmetazole) are slightly less effective against Gram-positive organisms and are somewhat more effective against Gram-negative organisms such as *Klebsiella*, *E coli*, and *Proteus* species. They are ineffective against *P aeruginosa*, *Actinobacter* species and a good number of obligate anaerobes. However cefoxitin and cefotetan, technically cephamycins (differentiated from true cephalosporins by the presence of a methoxyl

group in a specific location on the molecule) are effective against anaerobic Gram-negative organisms. Cefotetan is not, however, approved for use in children. The second generation cephalosporins are relatively resistant to β -lactamases, but are characterized by poor penetration of the blood-brain barrier. In human medicine, these second generation cephalosporins are commonly used in patients with pharyngitis, otitis media, lower respiratory tract infections, soft tissue infections, urinary tract infections and treatment of both human and animal bite wounds. Cefuroxime, cefaclor and cefprozil can be administered orally.

Third generation cephalosporins (ceftiofur, ceftriaxone, cefsulodin, cefotaxime, cefoperazone, ceforanide, ceftazidime, cefpodoxime, cefixime, ceftibuten, cefdinir, ceftizoxime) are the most active of the cephalosporins against Gram-negative aerobic organisms, effective against *Proteus vulgaris*, *Enterobacter* species, *Citrobacter* species, *Haemophilus* species, *Neisseria* species and *Moraxella* species. However these drugs exhibit only moderate activity against Gram-positive bacteria and are inferior in activity against staphylococci, although they are generally effective against penicillin resistant *Streptococcus pneumoniae*. Ceftazidime is the only third generation cephalosporin that is active against *P. aeruginosa*. Ceftiofur is recommended for treatment of bronchopneumonia in cattle, especially when caused by *Pasteurella hemolytica* or *P. aeruginosa*. The third generation cephalosporins are usually highly resistant to β -lactamases. Some third generation cephalosporins are effective in therapy for susceptible pathogens in bacterial meningitis, due to their ability to cross the blood-brain barrier. Ceftriaxone, cefotaxime and ceftazidime are used parenterally. Cefpodoxime, ceftibuten, cefdinir and cefixime can be given orally. Third generation cephalosporins are also used to treat bone and joint infections, pneumonia, enteritis, endocarditis, rhinosinusitis as well as cystitis.

The spectra of third and fourth generation cephalosporins vary and should be studied by the practitioner prior to initiating therapy. Cefepime is the only fourth generation cephalosporin approved in the United States for use in humans and has the most extended spectrum. Cefepime is effective against Gram-positive (including methicillin-susceptible *S. aureus*, α hemolytic streptococci, and some coagulase negative staphylococci) and Gram-negative organisms, including *P. aeruginosa*. The fourth generation cephalosporins feature chemical characteristics that may lead to reduced development of resistance by Gram-negative organisms.

The free base acid stable forms of cephalosporins are used for oral administration. Examples of oral preparations are cephalixin, cephradine, cefadroxil and cefachlor. Sodium salt derivatives are used for parenteral use. Cephalosporins are well distributed in most body fluids and tissues such as the kidneys, lungs, joints, bone and biliary tract; however, with the exception of some third generation cephalosporins, these drugs poorly penetrate the CSF.

***References available by request. Call the Infectious Disease Epidemiology Section, Office of Public Health, Louisiana Department of Health and Hospitals (504-219-4563)**